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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMBINATION THERAPY OF ZD6474 WITH 5-FU OR/AND CPT-11

(57) Abstract: The present invention relates to a method for the production of an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal such as a human, which is optionally being treated with ionising radiation, particularly a method for the treatment of a cancer, particularly a cancer involving a solid tumour, which comprises one of: the administration of ZD6474 in combination with 5-FU; the administration of ZD6474 in combination with CPT-11; and the administration of ZD6474 in combination with 5-FU and CPT-11; to a pharmaceutical composition comprising one of: ZD6474 and 5-FU; ZD6474 and CPT-11; and ZD6474 and 5-FU and CPT-11; to a combination product comprising one of: ZD6474 and 5-FU; ZD6474 and CPT-11; and ZD6474 and 5-FU and CPT-11, for use in a method of treatment of a human or animal body by therapy; to a kit comprising one of: ZD6474 and 5-FU; ZD6474 and CPT-11; and ZD6474 and 5-FU and CPT-11; to the use of one of: ZD6474 and 5-FU; ZD6474 and CPT-11; and ZD6474 and 5-FU and CPT-11, in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal such as a human which is optionally being treated with ionising radiation.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/4745 A61K31/513 A61K31/517 A61P35/00
 //(A61K31/517, 31:513), (A61K31/517, 31:4745)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, EMBASE, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/32651 A (HENNEQUIN LAURENT FRANCOIS AND ; THOMAS ANDREW PETER (GB); ASTRAZENeca) 10 May 2001 (2001-05-10) cited in the application page 26, line 22 - page 27, line 30 -----	1-14

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

S document member of the same patent family

Date of the actual completion of the international search

23 July 2004

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INTERNATIONAL SEARCH REPORT

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claim 14 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

PCT /GB2004/00055Q

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0132651	A	10-05-2001	
		AU 769222 B2	22-01-2004
		AU 1288601 A	14-05-2001
		BG 106659 A	31-03-2003
		BR 0015203 A	16-07-2002
		CA 2389767 A1	10-05-2001
		CN 1387527 T	25-12-2002
		CZ 20021526 A3	17-07-2002
		EE 200200237 A	16-06-2003
		EP 1244647 A1	02-10-2002
		WO 0132651 A1	10-05-2001
		HU 0203453 A2	28-05-2003
		JP 3522727 B2	26-04-2004
		JP 2003513089 T	08-04-2003
		NO 20022139 A	03-05-2002
		NZ 518028 A	26-03-2004
		PL 355942 A1	31-05-2004
		SK 6122002 A3	09-01-2003
		ZA 200202775 A	03-12-2003